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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LACOURCIERE, KAREN A	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 06/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/915,543	BASLER ET AL.	
	Examiner	Art Unit	
	Karen A. Lacourciere	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *71-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *71-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 03-25-2004 has been entered.

Claim Objections

Claim 71 is objected to because of the following informalities: the phrase "tcf-drive" in line 19 of the claim appears to be a typo and should be corrected to read "tcf-driven". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 71-78 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 71-78 are drawn to encompass polypeptides comprising a sequence consisting of residues 177-204 or residues 349-383 or residues 199-392 of SEQ ID NO:15, polypeptides comprising a sequence 90% identical to said sequences or polypeptides comprising a fragment of any of the afore mentioned polypeptides wherein the fragment encompasses a binding site for generally any anti-Bc19/hLgs antibody and wherein each of the polypeptides claimed inhibit tcf-driven luciferase activity in colon cancer cells.

The specification discloses polypeptides consisting of residues 177-204, residues 349-383 or residues 199-392 of SEQ ID NO:15, which correspond to domains within the human BCL9, and further discloses that polypeptides consisting of these regions have the activity of inhibiting tcf-driven luciferase activity in colon cancer cells. Polypeptides consisting of residues 177-204, residues 349-383 or residues 199-392 of SEQ ID NO:15, meet the written description provisions of 35 USC 112, first paragraph, because they meet both the structural and functional limitations of the claims, however, claims 71-78 are directed to encompass a much broader genus of polypeptides wherein the polypeptide comprises any one of the small homology regions specified and further possesses the function wherein the peptide inhibits tcf-driven luciferase in colon cancer cells. Each of the specifically claimed homology regions is a small peptide sequence comprised within a much larger polypeptide (e.g. each of these regions is a 28 amino acid sequence or 35 amino acid sequence comprised within the a full length polypeptide which is more than 1400 amino acids residues long). The claimed polypeptides encompass a large genus of polypeptide sequences comprising residues 177-204 or

residues 349-383 or residues 199-392 of SEQ ID NO:15, including full length polypeptides from other species, mutated versions of the full length polypeptide, polypeptides encoded by allelic variants and splice variants, derivatives and variants of these polypeptides, polypeptides comprising a fragment of unspecified length (e.g. even one amino acid residue of residues 199-392 of SEQ ID NO:15) wherein there is a common epitope with Bc19/hLgs and so forth and wherein the polypeptide inhibits tcf-driven luciferase activity in colon cancer cells. None of these amino acid sequences meet the written description provision of 35 USC 112, first paragraph, because the specification has not provided the skilled artisan with a written description sufficient to determine what polypeptides have this specific activity within the genus of polypeptides that meet the sequence limitations of the claim, nor has it even provided a written description that describes the full genus of polypeptides that meet the structural limitations of the claims (i.e. sequence) . Applicant has argued, and provided data that demonstrate (see for example figure 15B), polypeptides comprising the specific sequences do not necessarily also have the function of inhibiting tcf-driven luciferase activity in colon cancer cells. For example, additional sequences can interfere with this activity and, therefore, there is no direct correlation between the claimed structure and the claimed function. The specification has provided written description for the sequences, however, there is not sufficient written description to determine which polypeptides comprising these sequences meet the functional limitations. The specification provides insufficient written description to support the genus of polypeptides encompassed by the claim. For example, polypeptides comprising a

fragment of residues 199-392 of SEQ ID NO:15, wherein the fragment comprises a binding site for an anti-Bc19/hLgs antibody would potentially encompass polypeptides with a little as one amino acid in common with the species described by the specification and further, the skilled artisan could not envision what polypeptides meeting the structural limitations would also meet the functional limitations.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of polypeptides consisting of residues 177-204, residues 349-383 or residues 199-392 of SEQ ID NO:15, the skilled artisan cannot envision the detailed chemical structure of the encompassed proteins (or polynucleotides encoding such), regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood*

v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only polypeptides consisting of residues 177-204, residues 349-383 or residues 199-392 of SEQ ID NO:15, but not the full breadth of the claim, meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant and the specification has not provided a description of which polypeptides within the genus also have the function claimed. As supported by Applicant's arguments and data in the specification, there is not a reliable correlation between the structure provided

(sequence of the peptide fragments comprised within the claimed polypeptides) and the function claimed (inhibition of tcf-driven luciferase activity in colon cancer cells). Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 71-78 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al. (WO 01/57188).

Tang et al. disclose, and claim, an isolated polypeptide (SEQ ID NO: 2178 of Tang et al.) that is 99.4% identical to amino acid residues 1-1392 of the instantly disclosed human lgs/BCL9 protein (97% identical to the full length) (SEQ ID NO: 15 of the instant application) (see sequence alignment attached to the prior Office action mailed 03-11-2003), wherein the polypeptide comprises residues 177-204, residues 349-383 and residues 199-392 of SEQ ID NO:15 and wherein the polypeptide comprises a fragment comprises a binding site for an anti-Bc19/hLgs antibody . Tang et al. disclose their polypeptide as a chimeric protein, fused to a heterologous amino acid

sequence (see for example pages 27-34), including, for example, a GST moiety, a thioredoxin moiety, an antibody moiety and an epitope tag sequence (see for example page 31). Tang et al. disclose their polypeptide in a pharmaceutical composition, including wherein the protein is in a carrier facilitating the transport of the protein across a cell membrane (see for example, section 4.12.2 Compositions/Formulations). Tang et al. do not disclose their protein as inhibiting tcf-driven luciferase activity in colon cancer cells, however, they disclose their protein as a human BCL9 homologue and their protein meets all of the physical limitations of the claims and their protein is 97% identical (99.4% identical to residues 1-1392) to one embodiment of the claimed invention disclosed in the instant specification and further comprises the specific homology regions claimed and, therefore, would be expected to inhibit tcf-driven luciferase activity in colon cancer cells, as claimed.

Therefore, Tang et al. (WO 01/57188) anticipates claims 71-78.

Response to Arguments

Applicant's arguments filed 02-27-2004 have been fully considered but they are not persuasive. Applicant provides arguments directed to the rejections of record set forth in the prior Office action, mailed 11-28-2003, these arguments have been considered to the extent they read on the rejections of claim 71-78 set forth herein, but they have not been found persuasive.

The rejection of record under 35 U.S.C. 102(e) as being anticipated by Tang et al. (WO 01/57188) is maintained. Applicant argues that the activity of the polypeptide claimed is now "inhibition of tcf-driven luciferase activity" and that the experiment in

figure 15B provides evidence that the polypeptide of Tang et al. does not comprise that activity (see arguments filed 02-27-04, wherein Applicant argues that the polypeptide of Tang et al. corresponds to the polypeptide of Roose et al. (i.e. is 97% identical), which was used in the assay of figure 15B and does not have the ability to inhibit tcf-drive luciferase activity in colon cancer cells). In the Advisory Action dated 03-10-2004 it was stated that the rejection over Tang et al. would be withdrawn based on Applicant's statements that the peptide of Tang is identical to Roose et al., which was used in the experiment of Figure 15B, however, after further consideration it is unclear that Applicant is actually stating such. Applicant actually says that the Roose et al. polypeptide corresponds to the polypeptide of Tang et al. and is 97% identical. Further, upon reading the Roose et al. reference (Science, Vol. 285, 17 September 1999) it appears that the dominant negative polypeptide in Roose et al. is deleted in the β-catenin domain, which produces the dominant negative activity observed in the experiment of figure 15B of the instant application. The polypeptide disclosed by Tang et al., however, is not deleted in the β-catenin domain and, therefore, would not be expected to have the dominant negative phenotype of Roose et al. The evidence Applicant points to support their arguments does not appear to apply to the polypeptide disclosed by Tang et al. and, therefore, the rejection is maintained.

Given the very close identity of the polypeptide disclosed by Tang et al. to the physical characteristics of the claimed polypeptides and the preferred embodiment of the polypeptide disclosed in the specification, it would be expected that the polypeptide

disclosed by Tang et al. would inhibit tcf-drive luciferase activity in colon cancer cells, absent evidence to the contrary.

Applicant argues against the rejection of record under 35 USC 112, first paragraph, written description, by saying that it is the homology regions HD1 and HD2 which act to inhibit tcf-driven luciferase activity in colon cancer cells and the remaining sequences which may be present are not critical. This is not found to be persuasive because Applicant argues in response to the rejection under 35 USC 102(e) that additional sequences can actually eliminate that function, that, in fact, polypeptides that meet the structural limitations and comprise the homology domains do not actually possess the ability to inhibit tcf-driven luciferase activity in colon cancer cells. Further, Applicant's experiment in figure 15B support that additional sequences do change this activity, independent of the homology regions.

Applicant further argues that the % homology is directed to the peptide within the larger polypeptide and, therefore, the genus is not very large. This is not persuasive because the claimed polypeptide comprises the peptide and, therefore, the claimed polypeptide encompasses a highly variant genus of polypeptides.

Applicant argues that the peptide of amino acids 199-393 inherently inhibits tcf-driven luciferase activity in colon cancer cells, which contradicts Applicant's arguments that the Tang et al. polypeptide comprising amino acids 199-393 would not have the activity and the evidence that the Roose et al. polypeptide does not have such activity.

Applicant argues that part (iii) of claim 72 is directed to an epitope, which is typically a only 6-12 amino acids long, however, the claim is directed to a polypeptide

comprising an epitope and, therefore, the claims encompasses any polypeptide comprising a common epitope with the described embodiments and, therefore, encompasses polypeptides that comprise only a very small portion of that which was described (for example, possibly as little as 6-12 amino acids in common).

Applicant argues that the claims are directed to both structural and functional limitations and would not encompass the types of polypeptides with little homology to the described polypeptides as argued in the rejection of record. This is not found persuasive because the claims specification has not described polypeptides that meet the structural limitations of the claims and additionally meet the functional limitation of inhibiting tcf-driven luciferase activity in colon cancer cells. The arguments set forth by Applicant and the experimental evidence provided in the specification make it clear that even based on the structural requirements of the claims, function claimed does not reliably correspond to the structure provided.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (571) 272-0759. The examiner can normally be reached on Monday-Thursday 7:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (571) 272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Lacourciere
June 10, 2004

KAREN A. LACOURCIERE, PH.D
PRIMARY EXAMINER